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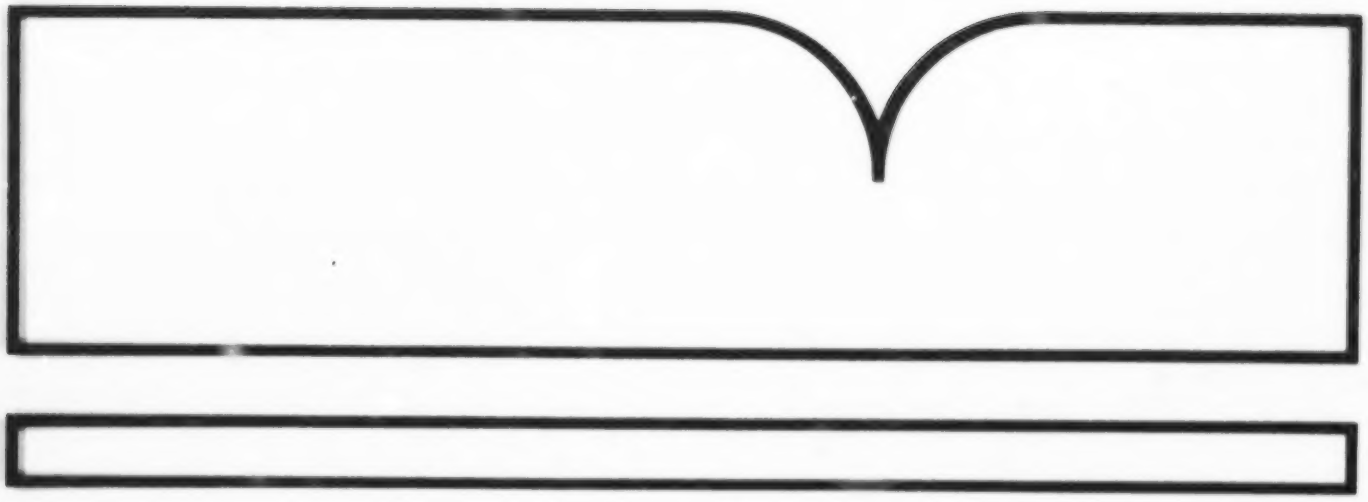

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16. ABSTRACT

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FUNDAMENTAL AND APPLIED TOXICOLOGY 7, 299–308 (1986)

Acute Toxicity of Pesticides in Adult and Weanling Rats[1]

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Acute Toxicity of Pesticides in Adult and Weanling Rats. GAINES, T. B., AND LINDER, R. E. (1986). *Fundam. Appl. Toxicol.* **7**, 299–308. LD50 values were determined for 57 pesticides administered by the oral or dermal route to adult male and female Sherman rats. Thirty-six of the chemicals were also tested by the oral route in one sex of weanlings. Nine pesticides tested by the oral route (bufencarb, cacodylic acid, dialifor, deltamethrin, dicamba, diquat, quintozene, phoxim, pyrazon) and four tested by the dermal route (bufencarb, chlordimeform, dichlofenthion, leptophos) were more toxic to females than to males whereas famphur and 2,4,5-T (oral route) were less toxic to females. Eighteen of the test chemicals were more toxic to the adult than to the weanling and four compounds (leptophos, methidathion, pyrazon, and sulfoxide) were more toxic to the weanling. In additional studies the variability of the LD50 value over a 1-year period was examined for two typical insecticides. Six consecutive bimonthly oral LD50 determinations for parathion and DDT in adults of both sexes indicated that the LD50 values were little affected by the time of year that the tests were done. 1986 Society of Toxicology.

The LD50 is commonly used to express the relative hazard associated with the acute toxicity of a substance. Since the LD50 value is influenced by variables such as species, strain, and test method (Hayes, 1975), the best estimates of relative toxicity are derived from data collected in a single species and strain under identical conditions. We have previously reported acute oral and dermal LD50 values for 98 pesticides and two metabolites of DDT in the adult Sherman rat (Gaines, 1960, 1969). In the present report, LD50 values for 57 additional pesticidal chemicals are given (chemicals are identified by common and chemical name and CAS No. in Table 1). In addition to LD50 values in adults, oral LD50 values are given for 36 of the compounds which were also tested in one sex of weanling animal. Many of these and earlier LD50 tests have been done in different years and in various months of the year. As an indication of possible change in the susceptibility of the rat colony to poisoning, annual LD50 tests of pp'DDT in male rats have been routinely conducted (Gaines, 1969). The current studies also include a series of LD50 tests on parathion and DDT which were done to examine the variability in the LD50 value with respect to time of year.

The values for acute toxicity reported here represent the final compilation of data for the LD50 test program whose purpose was to establish a reliable data base on the relative toxicities of pesticidal chemicals in rats, and to obtain other pertinent information including the type, onset, and duration of toxic effects following a single dose. The Environmental Protection Agency is no longer recommending the traditional LD50 for routine testing. Newer approaches to the evaluation of acute toxicity with minimum expenditure of ani-

[1] This paper has been reviewed by the Health Effects Research Laboratory, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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mal life are encouraged by the Agency (EPA, 1984).

METHODS

In general, the methods and procedures used were the same as those used in earlier work (Gaines, 1960, 1969). Except as indicated the compounds were technical grade and were dissolved or suspended in peanut oil for oral dosing (stomach tube) or in xylene for dermal application to the freshly shaved shoulder and back area. Whenever possible the compounds were formulated in varying concentrations and administered in volumes of 5 and 1.6 ml/kg body weight for oral and dermal dosing, respectively. Because of low toxicity or poor solubility of some of the compounds, it was sometimes necessary to adjust the dose volumes as indicated.

The Sherman strain rat used in the current studies was a specific-pathogen-free (SPF) version of the animal used previously. The rat colony was rederived via cesarean section and maintained under barrier conditions by the U.S. Centers for Disease Control, Atlanta, Georgia. Animals were transferred from the barrier facility at weaning and kept in conventional quarters until used. Adult animals were at least 90 days of age and weanlings were 4–6 weeks of age when tested. Minima of 10 animals per group and four dosage levels were used for each LD50 calculation. Limit tests on a single group of animals were utilized for compounds of low toxicity (LD50 greater than 5000 mg/kg) or when it was impractical to administer a single lethal dose. The animals were observed for at least 14 days after dosing or until recovered from signs of toxicity. LD50 values and related parameters were calculated using a computer based implementation of Finney's maximum likelihood probit technique (Lieberman, 1983).

In an additional series of LD50 tests, the variability of the LD50 values with respect to time of year was examined in adult male and female rats dosed with parathion and technical grade DDT at bimonthly intervals over a period of 1 year.

RESULTS

Table 2 gives the calculated LD50 values or estimate of the LD50 and, where applicable, the 95% confidence limits of the LD50, the slope of the dose–response curve, and the male/female and adult/weanling LD50 ratios. A ratio of greater than 1 indicates greater toxicity to the female compared to the male or greater toxicity to the weanling compared to the adult. The LD50 ratios are considered statistically different from 1 ($p < 0.05$) when the 95% confidence limits of the LD50 values do not overlap.

Based on nonoverlap of the 95% confidence limits of the LD50 values (Table 2) nine compounds tested by the oral route (bufencarb, cacodylic acid, dialifor, deltamethrin, dicamba, diquat, quintozene, phoxim, pyrazon) and four compounds tested by the dermal route (bufencarb, chlordimeform, dichlofenthion, leptophos) were more toxic to females than to males, while only famphur and 2,4,5-T (oral route) were less toxic to females. The range of male/female oral LD50 ratios was 0.55 (famphur) to 4.0 (dialifor). Male/female dermal LD50 ratios ranged from 0.75 (famphur) to 2.34 (leptophos). Two chemicals (cyhexatin and chlordimeform) appeared to be equally toxic by the oral and dermal routes while all others tested were less toxic by the dermal route. Eighteen of the compounds tested in weanling animals were less toxic to the weanling than to the adult and four compounds (leptophos, methidathion, pyrazon, and sulfoxide) were more toxic to the weanling. The lowest adult/weanling LD50 values for parathion or DDT was observed in female rats.

Table 3 gives the results of six consecutive bimonthly oral LD50 determinations for parathion and technical grade DDT. LD50 values for parathion ranged from 3.0 to 3.5 mg/kg in females and from 6.9 to 11.0 mg/kg in males. The 95% confidence interval for the minimum value in males (July) failed to overlap the test values for any other month. The ranges of LD50 values for DDT were 269–322 mg/kg in females and 218–268 mg/kg in males. The 95% confidence intervals for minimum and maximum LD50 values for DDT in males failed to overlap each other but each overlapped the values for all other test months. No difference in the bimonthly LD50 values for parathion or DDT was observed in female rats.

DISCUSSION

The data in the present report were accumulated over a period of several years. Peri-

TABLE 1

NAMES OF COMPOUNDS TESTED

Common name	Chemical name	CAS no.
Acephate	*O,S*-Dimethyl acetylphosphoramidothioate	30560-19-1
Dialifor	*S*-(2-chloro-1-Phthalimidoethyl)*O,O*-diethyl phosphorodithioate	10311-84-9
Dichlofenthion	*O*-2,4-Dichlorophenyl *O,O*-diethyl phosphorothioate	97-17-6
Leptophos	*O*-(4-bromo-2,5-dichlorophenyl)*O*-Methyl phenylphosphonothioate	21609-90-5
Methamidophos	*O,S*-Dimethyl phosphoramidothioate	10265-92-6
Methidathion	*S*-2,3-Dihydro-5-methoxy-2-oxo-1,3,4-thiadiazol-3-ylmethyl *O,O*-dimethyl phosphorodithioate	950-37-8
Phoxim	*O,O*-Diethyl α-cyanobenzylideneaminooxyphosphonothioate	14816-18-3
Famphur	*O*-4-Dimethylsulfamoylphenyl *O,O*-dimethyl phosphorothioate	52-85-7
Arsenic compounds		
Cacodylic acid	Dimethylarsinic acid	75-60-5
DSMA	Disodium methylarsonate	144-21-8
MAA	Methylarsonic acid	124-58-3
MSMA	Monosodium methylarsonate	2163-80-6
Carbamate compounds		
Bufencarb	Mixture of 3-(1-methylbutyl)phenyl methylcarbamate and 3-(1-ethylpropyl)phenyl methylcarbamate	8065-36-9
Carbanolate	6 Chloro-3,4-xylyl methylcarbamate	671-04-5
Carbofuran	2,3-Dihydro-2,2-dimethylbenzofuran-7-yl methylcarbamate	1563-66-2
Cycloate	*S*-Ethyl *N*-cyclohexyl-*N*-ethyl(thiocarbamate)	1134-23-2
Di-allate	*S*-2,3-Dichloroallyl diisopropyl(thiocarbamate)	2303-16-4
Methomyl	*S*-Methyl *N*-(methylcarbamoyloxy)thioacetimidate	16752-77-5
Propham	Isopropyl carbanilate	122-42-9
Others		
Ametryn	*N*-Ethyl-*N'*-isopropyl-6-methylthio-1,3,5-triazine-2,4-diyldiamine	834-12-8
Amitrole	1*H*-1,2,4-Triazol-3-ylamine	61-82-5
Atrazine	2-Chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine	1912-24-9
Bromacil	5-Bromo-3-*sec*-butyl-6-methyluracil	314-40-9
Captan	*N*-(trichloromethylthio)Cyclohex-4-ene-1,2,-dicarboximide	133-06-2
Chlordimeform	N^2-(4-chloro-*o*-tolyl)-N^1, N^1-Dimethylformamidine	6164-98-3
Chlorothalonil	Tetrachloroisophthalonitrile	1897-45-6
Cyhexatin	Tricyclohexyltin hydroxide	13121-70-5
Dalapon	2,2-Dichloropropanoic acid	75-99-0
Deltamethrin	(*S*)-α-Cyano-3-phenoxybenzyl(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate	52918-63-5
Dicamba	3,6-Dichloro-*o*-anisic acid	1918-00-9
Dichlorophen	4,4'-Dichloro-2,2'-methylenediphenol	97-23-4
Dicloran	2,6-Dichloro-4-nitroaniline	99-30-9
Dinoseb	2-*sec*-Butyl-4,6-dinitrophenol	88-85-7
Diquat	9,10-Dihydro-8a,10a-diazoniaphenanthrene dibromide monohydrate	6385-62-2
Diuron	3-(3,4-dichlorophenyl)-1,1-Dimethylurea	330-54-1
Endothall	7-Oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid	145-73-3
Etridiazol	5-Ethoxy-3-trichloromethyl-1,2,4-thiadiazole	2593-15-9
Fluorodifen	4-Nitrophenyl α,α,α-trifluoro-2-nitro-*p*-tolyl ether	15457-05-3
Folpet	*N*-(trichloromethylthio)Phthalimide	133-07-3
Hexachlorophene	2,2'-Methylene bis (3,4,6-trichlorophenol)	70-30-4
Linuron	3-(3,4-dichlorophenyl)-1-Methoxy-1-methylurea	330-55-2
Methazole	2-(3,4-dichlorophenyl)-4-Methyl-1,2,4-oxadiazolidine-3,5-dione	20354-26-1
Monuron	3-(4-chlorophenyl)-1,1-Dimethylurea	150-68-5
Nitrofen	2,4-Dichlorophenyl 4-nitrophenyl ether	1836-75-5
Para-dichlorobenzene	1,4-Dichlorobenzene	106-46-7
Piprotal	1-bis[2-(2-butoxyethoxy)Ethoxy]methyl-3,4-methylenedioxybenzene	5281-13-0
Prometon	*N,N'*-Diisopropyl-6-methoxy-1,3,5-triazine-2,4-diyldiamine	1610-18-0
Prometryne	*N,N'*-Diisopropyl-6-methylthio-1,3,5-triazine-2,4-diyldiamine	7287-19-6
Propazin	6-Chloro,*N,N'*-diisopropyl-1,3,5-triazine-2,4-diyldiamine	139-40-2
Pyrazon	5-Amino-4-chloro-2-phenylpyridazin-3(2*H*)-one	1698-60-8
Quintozene	Pentachloronitrobenzene	82-68-8
Resmethrin	5-Benzyl-3-furylmethyl(1*RS*,3*RS*; 1*RS*,3*SR*)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate	10453-86-8
Simazine	6-Chloro-*N,N'*-diethyl-1,3,5-triazine-2,4-diyldiamine	122-34-9
Sulfoxide	2-(1,3-benzodioxol-5-yl)Ethyl octyl sulfoxide	120-62-7
2,4,5-T	2,4,5-Trichlorophenoxy acetic acid	93-76-5
TCMTB	2-(thiocyanomethylthio) Benzothiazole	2593-15-9
Trifluralin	α,α,α-Trifluoro-2,6-dinitro-*N,N*-dipropyl-*p*-toluidine	1582-09-8

TABLE 2

ACUTE ORAL AND DERMAL TOXICITY OF PESTICIDAL COMPOUNDS IN RATS[a]

Common name	Age[b]	Sex	Route	LD_{50} (mg/kg)	95% C.L. (mg/kg)	Slope	LD_{50} (M/F)	Ratio (A/W)
Organic phosphorus compounds								
Acephate	A	M	Oral	1482	1266–1744	6.6		
	A	F	Oral	1652	1471–1919	7.5	0.90	
	W	M	Oral	1215	1096–1353	14.5		1.22
	A	M	Dermal	>2500[c]				
	A	F	Dermal	>2500[c]	•			
Dialifor	A	M	Oral	24	19–30	4.2		
	A	F	Oral	6	5–7	7.2	4.0*	
	W	M	Oral	39	34–44	10.3		0.62*
	A	M	Dermal	45	34–56	4.5		
	A	F	Dermal	28	24–34	5.5	1.61	
Dichlofenthion	A	M	Oral	185	172–200	12.3		
	A	F	Oral	172	144–202	7.7	1.08	
	A	M	Dermal	576	472–781	4.3		
	A	F	Dermal	355	297–422	7.3	1.62*	
Leptophos	A	M	Oral	19	17–23	7.4		
	A	F	Oral	20	18–23	9.2	0.95	
	W	F	Oral	12	9–14	6.1		1.67*
	A	M	Dermal	103	81–139	3.0		
	A	F	Dermal	44	32–64	3.9	2.34*	
Methamidophos	A	M	Oral	25	22–28	6.0		
	A	F	Oral	27	25–29	13.0	0.93	
	W	M	Oral	28	27–29	40.3		0.89
	A	M	Dermal	179[d]	140–217	3.8		
	A	F	Dermal	151[d]	119–186	6.3	1.19	
Methidathion	A	M	Oral	31	26–35	8.6		
	A	F	Oral	32	30–34	13.4	0.97	
	W	M	Oral	21	19–25	7.5		1.48*
	A	M	Dermal	94	76–106	10.3		
	A	F	Dermal	85	74–95	9.5	1.11	
Phoxim	A	M	Oral	363	332–396	15.8		
	A	F	Oral	300	291–312	32.1	1.21*	
	A	M	Dermal	1276[c]	1002–1576	4.8		
	A	F	Dermal	1224[c]	1084–1417	7.3	1.04	
Famphur	A	M	Oral	28	25–32	11.6		
	A	F	Oral	51	47–56	11.1	0.55*	
	W	F	Oral	73	66–87	7.0		0.70*
	A	M	Dermal	400	330–464	5.3		
	A	F	Dermal	533	409–664	5.2	0.75	
Arsenic compounds								
Cacodylic Acid	A	M	Oral	1315	1224–1428	9.6		
	A	F	Oral	644	555–734	8.3	2.04*	
	W	M	Oral	1433	1329–1544	8.8		0.92
DSMA[f]	A	M	Oral	928	832–1010	11.8		
	A	F	Oral	821	713–927	9.8	1.13	
	W	F	Oral	1698	1510–1879	10.1		0.48*

TABLE 2—*Continued*

Common name	Age[b]	Sex	Route	LD_{50} (mg/kg)	95% C.L. (mg/kg)	Slope	LD_{50} (M/F)	Ratio (A/W)
Arsenic compounds								
MAA	A	M	Oral	1101	1004–1202	11.1		
	A	F	Oral	961	868–1045	11.7	1.15	
	W	F	Oral	>2200				
MSMA[g]	A	M	Oral	1105	1060–1167	15.9		
	A	F	Oral	1059	986–1145	12.5	1.04	
	W	F	Oral	1746	1592–1896	10.5		0.61*
Carbamate compounds								
Bufencarb	A	M	Oral	97	88–105	12.7		
	A	F	Oral	61	58–65	19.3	1.60*	
	A	M	Dermal	237	205–269	8.2		
	A	F	Dermal	163	147–182	12.9	1.45*	
Carbanolate	A	M	Oral	44	36–52	5.1		
	A	F	Oral	36	30–43	6.6	1.22	
	A	M	Dermal	>1200[h]				
	A	F	Dermal	>1200[h]				
Carbofuran	A	M	Oral	9.0	8–11	5.4		
	A	F	Oral	8.0	7–9	6.1	1.13	
	A	M	Dermal	>1000[h]				
	A	F	Dermal	>1000[h]				
Cycloate	A	M	Oral	1838	1638–2013	10.1		
	A	F	Oral	1678	1548–1858	11.4	1.10	
	A	M	Dermal	2467[i]	2207–2744	12.3		
	A	F	Dermal	2502[i]	2256–2963	8.0	0.99	
Di-allate	A	M	Oral	684	640–749	15.1		
	A	F	Oral	750	673–831	15.5	0.91	
	A	M	Dermal	2175[i]	1933–2400	13.6		
	A	F	Dermal	2124[i]	1946–2317	13.7	1.02	
Methomyl	A	M	Oral	25	23–27	14.9		
	A	F	Oral	25	21–29	9.1	1.00	
	W	F	Oral	27	23–30	9.3		0.93
	A	M	Dermal	>2400[d]				
	A	F	Dermal	>2400[d]				
Propham	A	M	Oral	3724[j]	3113–4444	8.6		
	A	F	Oral	4315[j]	3721–5171	5.8	0.86	
	A	M	Dermal	>4000[h]				
	A	F	Dermal	>4000[h]				
Other compounds								
Ametryn	A	M	Oral	508	385–631	3.5		
	A	F	Oral	590	437–752	3.6	0.86	
	W	F	Oral	1630[k]	1298–2208	3.4		0.36*
	A	M	Dermal	>3000				
	A	F	Dermal	>3000				
Amitrole	A	M	Oral	>4080[l]				
	A	F	Oral	>4080[l]				
	A	M	Dermal	>2500[c]				
	A	F	Dermal	>2500[c]				
Atrazine	A	M	Oral	737	648–805	17.1		
	A	F	Oral	672	556–807	5.5	1.10	
	W	M	Oral	2310[k]	2152–2475	15.2		0.32*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				

TABLE 2—*Continued*

Common name	Age[b]	Sex	Route	LD_{50} (mg/kg)	95% C.L. (mg/kg)	Slope	LD_{50} (M/F)	Ratio (A/W)
Other compounds								
Bromacil	A	M	Oral	791	705–921	9.6		
	A	F	Oral	641	540–748	4.3	1.23	
	W	M	Oral	1737[k]	1392–2069	5.6		0.46*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Captan	A	M	Oral	>5000[n]				
	A	F	Oral	>5000[n]				
	W	F	Oral	>5000[n]				
Chlordimeform	A	M	Oral	301	255–352	6.7		
	A	F	Oral	265	223–302	4.6	1.14	
	A	M	Dermal	337	317–363	17.4		
	A	F	Dermal	263	235–295	7.7	1.28*	
Chlorothalonil	A	M	Oral	>5000[n]				
	A	F	Oral	>5000[n]				
	W	F	Oral	>5000[n]				
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Cyhexatin	A	M	Oral	779	519–1025	3.7		
	A	F	Oral	826	677–1005	5.7	0.94	
	W	F	Oral	561	421–693	4.1		1.47
	A	M	Dermal	767[m]	537–951	5.0		
	A	F	Dermal	446[m]	321–570	4.1	1.72	
Dalapon	A	M	Oral	7126	6629–7658	16.2		
	A	F	Oral	6936	6573–7204	20.1	1.03	
	A	M	Dermal	>5000[c]				
	A	F	Dermal	>5000[c]				
Deltamethrin	A	M	Oral	53	48–61	6.5		
	A	F	Oral	30	28–33	11.8	1.77*	
	W	F	Oral	48	42–54	6.2		0.63*
Dicamba	A	M	Oral	1404[o]	1251–1699	7.9		
	A	F	Oral	1039[o]	905–1164	7.0	1.35*	
	W	M	Oral	3294[o]	2984–3650	9.5		0.43*
Dichlorophen	A	M	Oral	1506	1310–1760	7.9		
	A	F	Oral	1683	1402–1986	5.9	0.89	
Dicloran	A	M	Oral	>4000[n]				
	A	F	Oral	>4000[n]				
Dinoseb	A	M	Oral	27	26–29	16.3		
	A	F	Oral	28	27–29	20.1	0.96	
	W	F	Oral	57	49–64	6.9		0.49*
Diquat	A	M	Oral	147	138–155	22.5		
	A	F	Oral	121	108–136	12.2	1.22*	
	A	M	Dermal	433[c]	344–568	4.3		
Diuron	A	M	Oral	1258	999–1583	4.2		
	A	F	Oral	1182	995–1450	4.6	1.06	
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Endothall	A	M	Oral	57	52–64	8.1		
	A	F	Oral	46	40–56	6.9	1.24	
	A	M	Dermal	>1000[c]				
	A	F	Dermal	>1000[c]				
Etridiazol	A	M	Oral	1310	1210–1494	12.0		
	A	F	Oral	1311	1248–1393	23.9	1.00	

TABLE 2—*Continued*

Common name	Age[b]	Sex	Route	LD_{50} (mg/kg)	95% C.L. (mg/kg)	Slope	LD_{50} (M/F)	Ratio (A/W)
Other compounds								
Fluorodifen	A	M	Oral	>5000[n]				
	A	F	Oral	>5000[n]				
	W	M	Oral	>5000[n]				
	A	M	Dermal	>2800				
	A	F	Dermal	>2800				
Folpet	A	M	Oral	>5000[n]				
	A	F	Oral	>5000[n]				
	W	F	Oral	>5000[n]				
Hexachlorophene	A	M	Oral	66	59–75	10.6		
	A	F	Oral	57	52–61	13.5	1.16	
	W	F	Oral	121	112–133	14.8		0.47*
Linuron	A	M	Oral	1146	982–1327	5.2		
	A	F	Oral	1508	1246–1934	6.2	0.76	
	W	M	Oral	2120[p]	1783–2325	9.5		0.54*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Methazole	A	M	Oral	777	635–930	6.9		
	A	F	Oral	925	766–1077	6.2	0.84	
	W	M	Oral	1903	1749–2154	9.6		0.41*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Monuron	A	M	Oral	1226	970–1642	4.2		
	A	F	Oral	1053	885–1249	4.6	1.16	
	W	M	Oral	2232[r]	1911–2568	5.2		0.55*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Nitrofen	A	M	Oral	2750[q]	2246–3559	5.6		
	A	F	Oral	2424[q]	2100–2727	7.9	1.13	
	A	M	Dermal	>5000				
	A	F	Dermal	>5000				
Para-dichlorobenzene	A	M	Oral	3863[s]	3561–4153	14.5		
	A	F	Oral	3790[s]	3425–4277	8.4	1.02	
	A	M	Dermal	>6000				
	A	F	Dermal	>6000				
Piprotal	A	M	Oral	2939[t]	2650–3301	8.8		
	A	F	Oral	3039[t]	2659–3507	7.6	0.97	
	A	M	Dermal	>5000[t]				
	A	F	Dermal	>5000[t]				
Prometon	A	M	Oral	503	411–600	5.8		
	A	F	Oral	511	430–612	7.3	0.98	
	W	M	Oral	2363[c]	1796–2915	5.8		0.21*
	A	M	Dermal	>2500				
	A	F	Dermal	>2500				
Prometryne	A	M	Oral	>4000[f]				
	A	F	Oral	>4000[f]				
	W	M	Oral	>4000[f]				
	A	M	Dermal	>2500				
	A	F	Dermal	>2500				
Propazin	A	M	Oral	>4000[f]				
	A	F	Oral	>4000[f]				
	W	M	Oral	>4000[f]				
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				

TABLE 2—*Continued*

Common name	Age[b]	Sex	Route	LD_{50} (mg/kg)	95% C.L. (mg/kg)	Slope	LD_{50} (M/F)	Ratio (A/W)
Other compounds								
Pyrazon	A	M	Oral	1311[k]	954–1744	4.7		
	A	F	Oral	647	545–793	6.7	2.03*	
	W	M	Oral	736	645–831	10.1		1.78*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Quintozene	A	M	Oral	1589[o]	1486–1776	12.2		
	A	F	Oral	1100[o]	1026–1165	13.8	1.45*	
	W	F	Oral	1362[o]	1256–1464	16.9		0.81*
	A	M	Dermal	>5000				
	A	F	Dermal	>5000				
Resmethrin	A	M	Oral	1244	885–1638	3.6		
	A	F	Oral	1721	1344–1957	9.9	0.72	
	W	M	Oral	1987[k]	1633–2338	5.5		0.63
	A	M	Dermal	>2500				
	A	F	Dermal	>2500				
Simazine	A	M	Oral	971	681–1244	3.8		
	A	F	Oral	973	818–1170	4.8	1.00	
	W	M	Oral	2367[k]	2035–2650	12.0		0.41*
	A	M	Dermal	>2500[m]				
	A	F	Dermal	>2500[m]				
Sulfoxide	A	M	Oral	3957	3066–5200	4.1		
	A	F	Oral	3477	3052–3884	10.1	1.14	
	W	M	Oral	2119	1834–2571	7.1		1.87*
2,4,5-T	A	M	Oral	342	330–359	35.1		
	A	F	Oral	410	375–458	9.5	0.83*	
	A	M	Dermal	1974[u]	1669–5109	8.1		
	A	F	Dermal	1535[u]	1342–1858	8.1	1.29	
TCMTB	A	M	Oral	781	691–909	9.1		
	A	F	Oral	831	738–939	10.2	0.94	
	W	F	Oral	1197	1123–1321	15.1		0.69*
Trifluralin	A	M	Oral	>5000				
	A	F	Oral	>5000				
	W	M	Oral	>3000				

[a] For oral dosing, water and oil soluble compounds were given as solutions in water or peanut oil and poorly soluble compounds were given as suspensions in peanut oil. For dermal dosing, compounds were usually dissolved in xylene. Dosage volumes were routinely 5–10 ml/kg for oral dosing and 1.6–10 ml/kg for dermal dosing. Exceptions to the above are noted.

[b] A = Adult; W = Weanling.

[c] In water.

[d] In ethanol.

[e] In xylene or undiluted technical grade.

[f] Ansar 8100 (80.1% DSMA).

[g] Ansar 170 H.C. (58.4% MSMA).

[h] In acetone.

[i] Undiluted technical grade.

[j] Dosage rates up to 20 ml/kg.

[k] Dosage rates up to 12 ml/kg.

[l] Dosage rate of 17 ml/kg.

[m] In propylene glycol suspension.

[n] Dosage rate of 20 ml/kg.

[o] Dosage rate of 15 ml/kg.

[p] Dosage rates up to 14 ml/kg.

[q] Dosage rates up to 13.3 ml/kg.

[r] Dosage rates up to 16.7 ml/kg.

[s] Dosage rates up to 16 ml/kg.

[t] Dosage rate of 16 ml/kg.

[u] In glycerol formal.

* $p < 0.05$.

TABLE 3

BIMONTHLY ORAL LD_{50} VALUES FOR PARATHION AND DDT

Compound	Sex	Month	LD_{50} (mg/kg)	95% Confidence interval of LD_{50} (mg/kg)	Slope
Parathion	F	March	3.4	3.1–3.6	21.6
	F	May	3.3	3.1–3.6	11.9
	F	July	3.0	2.6–3.3	10.1
	F	Sept.	3.0	2.8–3.3	12.3
	F	Nov.	3.5	3.3–3.7	17.4
	F	Jan.	3.1	2.9–3.4	17.0
Parathion	M	March	9.9	8.9–11.0	8.4
	M	May	10.2	9.2–11.1	8.8
	M	July	6.9	5.8–7.7	9.9
	M	Sept.	11.0	9.8–12.4	10.1
	M	Nov.	9.5	8.3–11.2	5.7
	M	Jan.	9.7	8.6–11.1	10.4
DDT	F	March	302	274–329	12.7
	F	May	270	243–302	8.4
	F	July	304	266–352	7.5
	F	Sept.	269	234–298	8.4
	F	Nov.	322	278–370	6.5
	F	Jan.	271	245–306	7.6
DDT	M	March	248	219–279	10.0
	M	May	229	198–260	9.6
	M	July	245	212–282	7.7
	M	Sept.	227	192–268	8.0
	M	Nov.	268	245–292	9.7
	M	Jan.	218	195–239	16.5

odically (usually annually) the oral LD50 of pp'DDT was determined in adult males as a means to monitor possible change in the susceptibility of the rat colony. LD50 values for pp'DDT (data not shown) obtained in the 2 years prior to rederivation of the colony were 150 and 142 mg/kg. Eight subsequent determinations in SPF rats (in mg/kg) were 182, 162, 170, 158, 142, 153, 135, and 142 with the 95% confidence limits overlapping for all LD50 values. Although altered susceptibility to other chemical types cannot be discounted, the similarity in response to DDT suggested that rederivation of the rat colony had little impact on toxicity. The serial LD50 values for parathion and DDT indicated good reproducibility over six consecutive bimonthly tests. Slight variations were noted in males for parathion in July and for DDT in January, but the deviations from the other values were not large. Although the data do not rule out possible seasonal influences on acute toxicity, LD50 values for parathion and DDT were little affected by the time of year that the tests were done.

Consistent with previous findings (Gaines, 1960, 1969) the female rat displayed a somewhat greater susceptibility to a number of the chemicals tested. The greater drug metabolizing activity of liver microsomes in the male rat (Kato, 1974) probably accounts for many of the sex-related differences in toxicity which are observed in this species. As expected, nearly all of the compounds were substantially less toxic by the dermal route than by the oral route.

Our results indicated some substantial differences in LD50 values in weanling versus

adult rats. The triazine compounds were particularly less toxic to the weanling with adult/weanling LD50 ratios of 0.21, 0.32, 0.36, and 0.41 for prometon, atrazine, ametryne, and simazine, respectively. A number of other studies have demonstrated that susceptibility to the toxicity of chemicals can vary with age. In experimental animals, data for therapeutic agents (Goldenthal, 1971) and pesticides (Lu *et al.*, 1965) indicate that many compounds are more toxic to the newborn than to the adult, although striking exceptions are not unusual. Pharmacokinetic factors thought to play an important role in age-related toxicity include differences in membrane permeability, distribution and excretion patterns, and the maturity of enzyme systems.

Of current concern is the risk assessment of pesticide exposure to prepubescent children and adolescents who are granted exemption to work in agriculture (EPA, 1980). Petersen (1980) in evaluating the toxicity of lithium chloride in several ages of rats by several routes of administration, found the chemical to be less toxic in 3- and 6-week-old rats than in adults when given orally, but similar in toxicity by intraperitoneal and subcutaneous routes. Brodeur and Dubois (1963) reported that 11 of 16 anti-cholinesterase insecticides administered by the intraperitoneal route were more toxic to the weanling rat than to the adult. In contrast, we found that, of 28 chemicals for which adult/weanling oral LD50 ratios were obtained, only 14% were more toxic to the weanling while 64% were more toxic to the adult. The route of exposure may be particularly important in developing animal models of age-related toxicity.

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